

indicate, however, that glycoprotein Ia, chemokine receptor 2, apolipoprotein C-III, and the G protein $\beta 3$ subunit are susceptibility loci for hypertension in Japanese men, and that tumor necrosis factor- α , insulin receptor substrate-1, and glycoprotein Ib α constitute such loci in Japanese women. Moreover, the combined genotypes for these polymorphisms may prove informative for determination of the genetic risk for hypertension. The genetic diagnosis system by the present inventors should therefore contribute to the primary prevention of hypertension and of cardiovascular diseases, stroke, or renal diseases induced by this condition.

[0068]

The present invention is not limited to the description of the above embodiments. A variety of modifications, which are within the scopes of the following claims and which are achieved easily by a person skilled in the art, are included in the present invention.

[0069]

[EFFECT OF THE INVENTION]

According to the present invention, gene polymorphisms associated with hypertension are analyzed and the genotype in a nucleic acid sample is detected. By using the information about the polymorphisms obtained by the detection of the genotype, diagnosis of the risk for hypertension with high accuracy and high predictability can be carried out. Therefore, the present invention provides an effective means for understanding in advance the risk of development of hypertension, so that it can be expected that the means should therefore contribute to the primary prevention of hypertension as well as to contribute the prevention of cardiovascular diseases, stroke, renal diseases, or the like, induced by hypertension. Furthermore, according to the present invention, auxiliary information useful for the diagnosis of hypertension can be obtained so as to enable an appropriate treatment and therefore prognosis can be improved. Furthermore, since the present invention provides useful information in elucidating the development mechanism of hypertension, it also provides an extremely important means for establishing a preventing method for hypertension.

[0070]

[SEQUENCE LISTING]

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<120> Method for diagnosing a risk of hypertension

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19

[BRIEF DESCRIPTION OF THE DRAWINGS]
[FIG. 1]

Figure 1 is a table summarizing 112 gene polymorphisms examined in a screening association study in Examples.

Figure 2 is also a table summarizing 112 gene polymorphisms examined in a screening association study in Examples.

Figure 3 is a table summarizing primers (SEQ ID NOs: 16, 17, 18, 14, 15, 11, 12, 13, 8, 9, 10, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 and 30 in this order from the top), probes (SEQ ID NOs: 31, 32, 33 and 34 in this order from the top) and other conditions used to determine the genotype in Examples. In Figure 3, FITC denotes fluorescein isothiocyanate, TxR denotes Texas Red and Biotin denotes biotin, respectively.

Figure 4 is a table summarizing single nucleotide polymorphisms examined in an association study in Examples.

Figure 5 is a table summarizing the background data of 1107 lesions in men and 833 lesions in women examined in an association study in Examples. Each data of age, body mass index, systolic blood pressure, diastolic blood pressure, and serum creatinine is represented by means \pm standard deviation. In table, *1 denotes $P < 0.0001$, *2 denotes $P < 0.001$, and *3 denotes $P < 0.01$, respectively.

Figure 6 is a table summarizing gene polymorphisms and results of multivariate logistic regression analysis examined in the association study. In each SNP, smaller P value is expressed in boldface.

Figure 7 is a view showing a distribution of genotype of gene polymorphisms associated with hypertension.

Figure 8 is a table showing results of stepwise forward selection method of multivariate logistic regression analysis of gene polymorphisms associated with hypertension.

Figure 9 is a table showing results of diagnosis of genetic risk for hypertension using a combination of four gene polymorphisms in men.

Figure 10 is a table showing results of diagnosis of genetic risk for hypertension using a combination of four gene polymorphisms in women.

Figure 11 is a graph showing a correlation between the cumulative odds ratio for hypertension and the number of single nucleotide polymorphisms. (A) shows the correlation in men and (B) shows the correlation in women. In (A), SNPs include: SNP1: GPIa (1648A \rightarrow G) polymorphism, SNP 2: CCR2 (190G \rightarrow A) polymorphism, SNP3: ApoC-III (1100C \rightarrow T) polymorphism, and SNP4: GP β 3 (825C \rightarrow T) polymorphism. In (B), SNPs include: SNP1: TNF α (-850C \rightarrow T) polymorphism, SNP2: TNF α (-238G \rightarrow A) polymorphism, SNP3: IRS-1 (3494G \rightarrow A) polymorphism, and

SNP4: GPIIb α (1018C \rightarrow T) polymorphism.